

## AMENDMENT TO THE SPECIFICATION

Please make the following amendments to the Specification.

Replace paragraph 0036 with the following paragraph:

Reference is now made to Fig.1, which is a simplified diagram describing each of a plurality of novel bioinformatically detected viral genes of the present invention, referred to here as Viral Genomic Address Messenger( VGAM) viral genes, which modulates expression of respective host target gene thereof, the function and utility of which host target genes is known in the art. VGAM is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA( miRNA) gene. The method by which VGAM was detected is described hereinabove with reference to Figs.2-8. VGAM GENE is a viral gene contained in the genome of a virus. VGAM HOST TARGET GENE is a human gene contained in the human genome. VGAM GENE encodes a VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM PRECURSOR RNA does not encode a protein. VGAM PRECURSOR RNA folds onto itself, forming VGAM FOLDED PRECURSOR RNA, which has a two-dimensional 'hairpin structure'. As is well known in the art, this 'hairpin structure', is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof. By "inversed-reversed" is meant a sequence which is reversed and wherein each nucleotide is replaced by a complementary nucleotide, as is well known in the art(e.g.ATGGC is the inversed-reversed sequence of GCCAT).An enzyme complex designated DICER COMPLEX, 'dices' the VGAM FOLDED PRECURSOR RNA into VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, 'dicing' of a hairpin structured RNA precursor product into a short~22 nt RNA segment is catalyzed by enzyme complex comprising an enzyme called Dicer together with other necessary proteins. VGAM HOST TARGET GENE encodes a corresponding messenger RNA, VGAM HOST TARGET RNA. VGAM HOST TARGET RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5' untranslated region, a protein coding region and a 3' untranslated region, designated 5'UTR, PROTEIN CODING and 3'UTR respectively. VGAM RNA binds complementarily to one or more host target binding sites located in untranslated regions of VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each

of the host target binding sites. As an illustration, Fig.1 shows 3 such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig.1 is meant as an illustration only, and is not meant to be limiting-VGAM RNA may have different number of host target binding sites in untranslated regions of a VGAM HOST TARGET RNA. It is further appreciated that while Fig.1 depicts host target binding sites in the 3'UTR region, this is meant as an example only-these host target binding sites may be located in the 3'UTR region, the 5'UTR region, or in both 3'UTR and 5'UTR regions. The complementary binding of VGAM RNA to host target binding sites on VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, Inhibits translation of VGAM HOST TARGET RNA into VGAM HOST TARGET PROTEIN.VGAM HOST TARGET PROTEIN is therefore outlined by a broken line. It is appreciated that VGAM HOST TARGET GENE in fact represents a plurality of VGAM host target genes. The mRNA of each one of this plurality of VGAM host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM RNA, and which when bound by VGAM RNA causes inhibition of translation of respective one or more VGAM host target proteins. It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig.1 with specific reference to translational inhibition exerted by VGAM GENE on one or more VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes( primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., 'Perspective:Glimpses of tiny RNA World' Science 294, 779 (2001)). It is yet further appreciated that a function of VGAM is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host . Accordingly, utilities of VGAM include diagnosis, prevention and treatment of viral infection by a virus. Specific functions, and accordingly utilities, of VGAM correlate with, and may be deduced from, the identity of the host target genes which VGAM binds and inhibits, and the function of these host target genes, as elaborated hereinbelow. Nucleotide sequences of the VGAM PRECURSOR RNA, and of the 'diced' VGAM RNA and a schematic representation of the secondary folding of VGAM FOLDED PRECURSOR RNA of each of the plurality of VGAM GENES described by Fig. 1 are further described hereinbelow-with reference to Table 1. For example, ~~Nucleotide-nucleotide~~ sequences

of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE -III of Fig.1, found on , and schematic representation of the complementarity of each of these host target binding sites to VGAM RNA (VGAM2191) are described hereinbelow with reference to Table 2.

Replace paragraph 0044 with the following paragraph:

Fig. 6B is a simplified flowchart illustrating training of a dicer-cut location detector constructed and operative in accordance with a preferred embodiment of the present invention. Figure 6C is a simplified flowchart illustrating prediction of a viral genomic address messenger.

Replace paragraph 0048 with the following paragraph:

Reference is now made to Fig.9, which is a simplified diagram describing each of a plurality of novel bioinformatically detected regulatory viral genes, referred hereto as Viral Genomic Record(VGR) viral genes, which encodes an 'operon-like ' cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art. VGR GENE is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR GENE was detected is described hereinabove with reference to ~~Figs.6-15~~ Fig. 6-14. VGR GENE encodes VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long. VGR PRECURSOR RNA folds spatially, forming VGR FOLDED PRECURSOR RNA. It is appreciated that VGR FOLDED PRECURSOR RNA comprises a plurality of what is known in the art as 'hairpin' structures. These 'hairpin' structures are due to the fact that the nucleotide sequence of VGR PRECURSOR RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art. VGR FOLDED PRECURSOR RNA is naturally processed by cellular enzymatic activity into a plurality of separate VGAM precursor RNAs, schematically represented by VGAM1 PRECURSOR, VGAM2 PRECURSOR, VGAM3 PRECURSOR, VGAM4 PRECURSOR, VGAM5 PRECURSOR, VGAM6 PRECURSOR, VGAM7 PRECURSOR, and VGAM8 PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM PRECURSOR RNA of Fig. 8. The above mentioned VGAM precursor RNA are diced by DICER COMPLEX of Fig.8, yielding respective short RNA segments of about 22 nucleotides in length, schematically represented as VGAM1 RNA, VGAM2 RNA,

VGAM3 RNA, VGAM4 RNA, VGAM5 RNA, VGAM6 RNA, VGAM7 RNA and VGAM8 RNA, respectively, each of which VGAM RNAs corresponding to VGAM RNA to Fig.8 VGAM1 RNA binds complementarily to a host target binding site located in an untranslated region of VGAM1 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig.10, thereby inhibiting translation of VGAM1 HOST TARGET RNA into VGAM1 HOST TARGET PROTEIN, both of Fig.10. VGAM2 RNA binds complementarily to a host target binding site located in an untranslated region of VGAM2 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II, or BINDING SITE III of Fig.10, thereby inhibiting translation of VGAM2 HOST TARGET RNA into VGAM2 HOST TARGET PROTEIN, both of Fig.10. VGAM3 RNA binds complementarily to a host target binding site located in an untranslated region of VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig.10, thereby inhibiting translation of VGAM3 HOST TARGET RNA into VGAM3 HOST TARGET PROTEIN, both of Fig.10. VGAM4 RNA binds complementarily to a host target binding site located in an untranslated region of VGAM4 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig.10, thereby inhibiting translation of VGAM4 HOST TARGET RNA into VGAM4 HOST TARGET PROTEIN, both of Fig. 10. VGAM5 RNA binds complementarily to a host target binding site located in an untranslated region of VGAM5 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig.10, thereby inhibiting translation of VGAM5 HOST TARGET RNA into VGAM5 HOST TARGET PROTEIN, both of Fig.10. VGAM6 RNA binds complementarily to a host target binding site located in an untranslated region of VGAM6 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig.10, thereby inhibiting translation of VGAM6 HOST TARGET RNA into VGAM6 HOST TARGET PROTEIN, both of Fig.10. VGAM7 RNA binds complementarily to a host target binding site located in an untranslated region of VGAM7 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig.10, thereby inhibiting translation of VGAM7 HOST TARGET RNA into VGAM7 HOST TARGET PROTEIN, both of Fig.10. VGAM8 RNA binds complementarily to a host target binding site located in an

untranslated region of VGAM8 HOST TARGET RNA which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig.10, thereby inhibiting translation of VGAM8 HOST TARGET RNA into VGAM6 HOST TARGET PROTEIN, both of Fig.10. It is appreciated that a function of VGR GENE is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR GENE include diagnosis, prevention and treatment of viral infection by a virus. Specific functions, and accordingly utilities, of VGR GENE correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNA comprised in the 'operon-like' cluster of VGR GENE, schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM8 HOST TARGET PROTEIN.

Replace paragraph 0086 with the following paragraph:

The present invention discloses 3815 novel viral genes of the VGAM group of genes, which have been detected bioinformatically, as described hereinbelow with reference to Tables 1 and 2 for VGAM2191. Laboratory confirmation of 4 genes of the GAM group of genes is described hereinbelow with reference to Figs. 12 through 14.

Replace paragraph 0127 with the following paragraph:

GR GENE (Genomic Record Gene) is gene of a novel, bioinformatically detected group of regulatory, non protein coding, RNA genes. The method by which GR is detected is described hereinabove with reference to ~~FIGS 6-15~~ Figs. 6-14.

Replace paragraph 0134 with the following paragraph:

The present invention discloses 50443 novel viral genes of the GR group of genes, which have been detected bioinformatically, as described hereinbelow with reference to Tables 1 and 2 for VGAM2191. Laboratory confirmation of 3 genes of the GR group of genes is described hereinbelow with reference to Figs.9A through 14.

Replace paragraph 0137 with the following paragraph:

The present invention discloses a first plurality of novel genes referred to here as VGAM genes, and a second plurality of operon-like genes referred to here as GR genes, each of the GR genes

encoding a plurality of VGAM genes. The present invention further discloses a very large number of known target –genes , which are bound by, and the expression of which is modulated by each of the novel genes of the present invention . Published scientific data referenced by the present invention provides specific, substantial, and credible evidence that the abovementioned target genes modulated by novel genes of the present invention, are associated with various diseases. Specific novel genes of the present invention, target genes thereof and diseases associated therewith, are described hereinbelow with reference to Tables 1 and 2 for VGAM2191. It is therefore appreciated that a function of VGAM genes and GR genes of the present invention is modulation of expression of target genes related to known diseases, and that therefore utilities of novel genes of the present invention include diagnosis and treatment of the above-mentioned diseases. Fig. 10 describes various types of diagnostic and therapeutic utilities of novel genes of the present invention.

Delete paragraphs 0174 to 030614

Following paragraph 030627, please add the following table.

**Table 1**

GENE	PRECURSOR	P-	GENE	G-	FOLDED	PRECURSOR
	-SEQUENCE	SEQID	-SEQ	SEQID		
=====	=====	=====	=====	=====	=====	=====
GAM	GTACTGGGTC	2194	TCTCT	5264	c	c
2191	TCTCTGGTTA		GGTTA		gta tgggt tctctggtttag ccaga	tct ct g
	GACCAGATCT		GACCA			gagc g
	GAGCCTGGGA		GATCT		cgt accca agggatcaatc ggtct	ctcg g
	GCTCTCTGGC		GAGC		c - - - -	ag
	TAACTAGGGA					
	ACCCACTGTC					

Following paragraph 03628, please add the following table.

**Table 2**

GENE	TARGET	UTR	SEQUENCE	SEQID	BINDING-SITE
=====	=====	---	=====	=====	=====
GAM2191	ITGA5	3'	CCTCTGTCCCTGGATCTGAG	41496	GTTAGA A_
					TCTCTG CC GATCTGAG
					GGAGAC GG CTAGACTC
					AG_____ AC
GAM2191	SCD	3'	CTCTTGATCAGATCTGAG	22825	- TAGAC
					CTCT GGT CAGATCTGAG
					GAGA CTA GTCTAGACTC
					A _____
GAM2191	SF3B3	3'	TCTGGTTAGATTCTAGAGC	29681	CCAGA -
					TCTGGTTAGA TCT GAGC

GAM2191	SLC22A11	3'	TCTCTGGTTGGCGTGGCTGAG	32965	<pre>       AGACCAATCT A_____T AGACCAGAT TCTCTGGTT      CTGAG       AGAGACCAA            GACTC CCGCACC_ AC  A TCTGGTTAG  CAG TCTGAGC       AGACCAATT  GTT AGACTCG _____G AGAC  A TCTCTGGTT  CAG TCTGAG       AGAGACTAA  GTC AGACTC _____C AACC TAACTAGGG  CACTG       GTTGATCTC  GTGAC </pre>
GAM2191	SLC4A4	3'	TCTGGTTAACAACCTCTGAGC	19065	<pre> TCTGGTTAG  CAG TCTGAGC       AGACCAATT  GTT AGACTCG _____G AGAC  A TCTCTGGTT  CAG TCTGAG       AGAGACTAA  GTC AGACTC _____C AACC TAACTAGGG  CACTG       GTTGATCTC  GTGAC </pre>
GAM2191	ZNF180	3'	TCTCTGATTGAGGTCTGAG	29936	<pre> TCTCTGGTT  CAG TCTGAGC       AGAGACTAA  GTC AGACTC _____C AACC TAACTAGGG  CACTG       GTTGATCTC  GTGAC </pre>
GAM2191	AKAP13	3'	CAACTAGAGCACTG	28470	<pre> TAACTAGGG  CACTG       GTTGATCTC  GTGAC </pre>
GAM2191	DNAH11	3'	CTAGAAAATCCTCACTGC	19096	<pre> GG _ _ CTAG  AA CC CACTGC                   GATC  TT GG GTGACG TT  A  A _ CCC TAACTAGG  GAA  ACTG       ATTGATCC  CTT  TGAC A  A_ T  C_ _ TAAC AGGGAAC  CAC  TGC             ATTG TCCCTTG  GTG  ACG _ TA  TA </pre>
GAM2191	FGFR2	3'	TAACTAGGTGAATACTG	35667	<pre> _ CCC TAACTAGG  GAA  ACTG       ATTGATCC  CTT  TGAC A  A_ T  C_ _ TAAC AGGGAAC  CAC  TGC             ATTG TCCCTTG  GTG  ACG _ TA  TA </pre>
GAM2191	GTF2E2	3'	TAACAGGGAACATCATTGC	13318	<pre> T  C_ _ TAAC AGGGAAC  CAC  TGC             ATTG TCCCTTG  GTG  ACG _ TA  TA </pre>
GAM2191	ILK	3'	CAACCAGAGCCTGCTGC	21122	<pre> AA CA TAACTAGGG  CC  CTGC       GTTGGTCTC  GG  GACG C_ AC T  GAA AAC AGG  CCCACTGC             TTG TCC  GGGTGACG </pre>
GAM2191	KIF3B	3'	AACAGGCCCACTGC	22027	<pre> T  GAA AAC AGG  CCCACTGC             TTG TCC  GGGTGACG </pre>
GAM2191	MAP1B	3'	ACTAAAGAATGCCTACTGC	25389	<pre> _ C ACTAGGGAA  CC  ACTGC       TGATTCTT  GG  TGACG AC  A AACC _ TAACTAGGG  CA  CTGC       GTTGATCCC  GT  GACG CTTA  A _ C_ AAGTAGGG  AAC  CACTG       TTGATCCC  TTG  GTGAC ATA  AA T  G _ C AGG AA  CCCACTGC                C TCC TT  GGGTGACG T  G TC GAA  CA TAACTAGG  CC  CTGC </pre>
GAM2191	MLH3	3'	CAACTAGGGGAATCATCTGC	30778	<pre> TAACTAGGG  CA  CTGC       GTTGATCCC  GT  GACG CTTA  A _ C_ AAGTAGGG  AAC  CACTG       TTGATCCC  TTG  GTGAC ATA  AA T  G _ C AGG AA  CCCACTGC                C TCC TT  GGGTGACG T  G TC GAA  CA TAACTAGG  CC  CTGC </pre>
GAM2191	MYO1A	5'	AACTAGGGTATAACTTCACTG	23919	<pre> AAGTAGGG  AAC  CACTG       TTGATCCC  TTG  GTGAC ATA  AA T  G _ C AGG AA  CCCACTGC                C TCC TT  GGGTGACG T  G TC GAA  CA TAACTAGG  CC  CTGC </pre>
GAM2191	POMZP3	3'	GAAGGCAAAGCCCACTGC	29241	<pre> T  G _ C AGG AA  CCCACTGC                C TCC TT  GGGTGACG T  G TC GAA  CA TAACTAGG  CC  CTGC </pre>
GAM2191	TRPM2	5'	CAACCAGGCCTGCTGC	17687	<pre> TAACTAGG  CC  CTGC </pre>

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GTTGGTCC  GG  GACG
      ____ AC

GAM2191  UTY      3'  TAACTAAGGAAAATTCTGC      28314      CCA
                                TAACTAGGGAA      CTGC
                                |||||
                                ATTGATTCCTT      GACG
                                TTAA
GAM2191  YWHAZ    3'  CAACTAAGGAGAGATTGCTGC      18201      ACCCA
                                TAACTAGGGA      CTGC
                                |||||
                                GTTGATTCCT      GACG
                                CTCTAAAC
GAM2191  ZP3A     3'  GAAGGCAAAGCCCACTGC      28385      T  G  ____
                                C  AGG  AA  CCCACTGC
                                |  |||  ||  |||||
                                C  TCC  TT  GGGTGACG
                                T    G  TC

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Delete paragraphs 030629-49618.

Delete paragraphs 49628-194259.

Delete the 9700 page-long tabular section at the end of the specification.

Delete Tables 1 and 2, which were submitted on compact discs.